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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/026,651	Applicant(s) STAMFORD ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *5-11 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 21-31* is/are rejected.

7)☒ Claim(s) *12-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 1-4, 12-14, and 21-31 in Paper No. 4 is acknowledged. Claims 1-4, 12-14, and 21-31 will be examined to the extent they embrace the elected subject matter. Claims 5-11 and15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter.

The traversal is on the ground(s) that the claims 1-31 form a part of the one and same invention and that same art search will most probably apply to alleged separate inventions. This is not found persuasive because reasons of record. The following apply to applicants' traversal.

Applicants' argument that they are puzzled by the restriction requirement and that the claims 1-31 form a part of the one and same invention and that same art search will most probably apply to alleged separate inventions, is totally incorrect.

As per MPEP § 803,there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent or distinct as claimed and

(B) There must be a serious burden on the examiner if restriction is required.

Instant claims meet both these criteria as clearly stated in the previous office action. To repeat:

The inventions are distinct, each from the other because of the following reasons:

Invention I, II, III, IV, V, VI and VII are independent and distinct from each other because they are directed to structurally dissimilar compounds that lack common core namely isomeric pyridine versus pyrazine versus isomeric pyrimidines versus pyridazine versus thiophene versus thiazole and many other hetero rings. Consequently, the groups have different classifications and require separate prior art searches. They can be made and used independently. Art, which may render obvious or anticipate one of the groups would not necessarily do the same for the other group. See for example Kabbe et al. provided in the IDS. Each can support a patent, as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group.

In addition, it is necessary to classify and search all the hetero cores and such a search of all core s would serious search burden given the limited time available for each application.

Contrary to applicants' urging, it would not be possible to a single search and expect that the search would cover all the core groups embraced in the instant claims.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 21-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply.

1. Recitation of the term "prodrug' in claims 1-4 and 21-31 is deemed as indefinite for more than one reason. Prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of prodrugs is acceptable and would include esters, amides alkoxycarbonyl etc. However, claims 1-4 and 21-31 also include in addition to prodrugs, esters, amides, alkoxycarbonyl etc which are by definition included in prodrugs. Therefore it is not clear what is the difference between these variable groups and the prodrug groups.

Furthermore, if one were assume that the prodrug of instant claims are derived form hydroxyl, carboxyl groups recited in definition of varible groups of formula I, then hydroxy and carboxy bearing compounds should be active compound and their prodrugs inactive by definition. But careful look at the claims show that applicants are claiming the esters as active compounds. See COOR groups recited at various places in these claims. Hence the term "prodrug" imparts ambiguity to the meaning and scope of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for eating disorder, does not reasonably provide enablement for any or all metabolic disorders including those yet to be discovered as due to neuropeptide Y Y5 receptor activity. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claims, which are drawn to a method for treating metabolic disorders, are not adequately enabled for the range of disorders generically recited therein. From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves antagonism of NPY receptor, would be useful for all sorts of metabolic disease. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended mammal. That a single class of compounds can be used to treat all disorders generically embraced in the claims is an incredible finding for which applicants have not provided supporting evidence. Moreover many if not most of metabolic disorders due to inborn error are very difficult to treat as claimed herein. Note substantiation of utility and its scope is required when utility is "sufficiently unusual" "speculative", or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly

claimed 'treatment effect solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. In evaluating the enablement question, several factors are to be considered.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention:

The method of use claims are drawn to treatment of any and all metabolic disorders diseases, including those yet to be discovered. However, specification provides no support for treating all or any metabolic disorders/ diseases. Specification has not provided any evidence or nexus that because of the mode of action of the instant compound viz. antagonism of neuropeptide receptor Y5, the compound would be useful for treating all or any metabolic disorders.

2) The state of the prior art:

There are no known compounds of similar structure, which have been demonstrated shown to be useful for treating all or any metabolic diseases. For example, the notion that a compound could be effective against all or any metabolic diseases because of its in interaction with a single target in the instant case viz. NPY Y5

receptor, in general, is absolutely contrary to our current understanding of pharmacological basis of drug design and treatment of diseases. In fact a specific target is often chosen to treat a specific disease or that specific target related diseases. Furthermore, even the recent references do not support treatment of all metabolic disorders. For examples note a) Betancur et al., (TIPS Vol. 18, 372-386,1997) which reviews neuropeptide receptors and their antagonists, does not teach treatment of all or any disease. See pages 378-379. b) Wieland et al., (Expert Opin. Investig. Drugs 9(6): 1327-1346,2000, PubMed Abstract provided.) describes role of NPY Y1 and Y5 receptor antagonist for human obesity but does suggest for treating any or all metabolic diseases.

3) The predictability or lack thereof in the art:

As noted above, although there several prior art which teach similar compounds as viz. regulating the effect of neuropeptide receptor, they do not teach use of the compound disclosed for treating any or all disorders as claimed and hence there is no art predictability or assurance that instant compound would do so.

4) The amount of direction or guidance present:

Specification provides no guidance or direction as to how would one use the instant compound to treat all or any metabolic disorder due to NPY Y5 activity.

5) The presence or absence of working examples:

There are no working examples to show that how the instant compound could be used to treat metabolic disorders other than those stated above wherein neuropeptide Y is implicated as causative agent.

6.The breadth of the claim:

The breadth of the claim is broad enough to include treatment of any or all metabolic disorders including those yet to be discovered for which there is no pharmacological basis or showing in the specification.

7) The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

Claim Objections

Claim 30 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 21. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Allowable Subject Matter

Claims 12-14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims would be allowed since specific

species embraced in these claims are not taught or suggested by the art of record or from a search in the relevant art area.

References cited in the Information Disclosure Statement (paper # 2) are made of record.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

5/15/2003